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EXAMINER

WILDER, CYNTHIA B

ART UNIT PAPER NUMBER

1637

DATE MAILED: 12/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/035,042	Applicant(s) KRYLOV ET AL.	
	Examiner Cynthia B. Wilder, Ph.D.	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 October 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date: _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____ |

FINAL ACTION

1. Applicant's amendment filed on October 5, 2004 is acknowledged. Claims 1, 8, 9 have been amended. Claims 17-23 have been canceled. Claims 1-16 is pending in the instant invention. All of the amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons noted below.

Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Rejections

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The claim rejections under 35 USC 112 second paragraph directed to claims 1-14, 17 and 19-21 is withdrawn in view of Applicant's amendment. The claim rejection under 35 USC 102(b) directed to claims 1-5, 7-9, 12-13 as being anticipated by Guschin et al is withdrawn in view of Applicant's amendment. The prior art rejection under 35 USC 102(e) directed to claims 1, 4, 5 and 7 as being anticipated by Taylor et al is maintained and discussed below. The prior art rejection under 35 USC 102(a) directed to claims 17, 19-23 as being anticipated by Arenkov et al is withdrawn in view of Applicant's cancellation of claims 17-23. The prior art rejection under 35 USC 103(a) directed to claims 1-14 as being obvious over Wang et al in view of Drobyshev et al and further in view of Arenkov et al is maintained and discussed below. The prior art

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rejection under 35 USC 103(a) directed to claims 17, 19-21 as being obvious over Wang et al in view of Drobyshev et al and further in view of Arenkov et al is withdrawn in view of Applicant's cancellation of the claims. The prior art rejection under 35 USC 103(a) directed to claims 15 and 16 as being obvious over Guschin et al is maintained and discussed below.

Claim Rejections - 35 USC § 102(e)

4. Once again, claims 1, 4, 5, 7 are rejected under 35 U.S.C. 102(e) as being anticipated by Taylor et al (US 6682893, Effective filing date January 1998). Regarding claims 1, 4, 5 and 14, Taylor et al. teach a method comprising immobilizing a nucleic acid (RNA, ss DNA or ds DNA) or a protein within a solid support wherein said solid support is a gel pad; contacting the immobilized nucleic acid and/or immobilized protein under conditions that allow the nucleic acid in an aqueous solution and/or the protein in an aqueous to interact and measuring the interaction of the nucleic acid and/or protein interaction via fluorescence (col. 7, lines 21-30 and col. 8, lines 28-42). Therefore, Taylor et al meets all of the limitations of claims 1, 4, 5, 7 of the instant invention.

Applicant's Traversal

5. Applicant summarizes the invention as defined by amended independent claim 1. Applicant contends that the amended independent claim 1 distinguished over the cited reference at least by requiring the nucleic acid or protein contacted with the nucleic acid or protein contacted with the immobilized protein or nucleic acid, respectively, to be in aqueous solution. Applicant contends that by contrast Taylor et al fail to disclose this element and therefore fail to teach every element of the claimed method. In Taylor et al, as demonstrated by col. 7, lines 21-

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30 and col. 8 38-42, both nucleic acids and/or proteins are immobilized in separate layers of a gel, forcing the interaction to place within two gel layers, such that disclosed by Taylor et al., may increase the concentration effect, thus producing artificial results, or require higher concentration of material, this making the method impractical for use in assay where only small amounts of material can be obtained. Paragraph (0023) of the current specification states that it was surprising and unexpected that "meaningful data can be obtained [with the methods of the invention] utilizing infinitesimal amounts of protein and/or nucleic acids. Applicant states that furthermore, the use additional gel layers require additions searcher time and labor. Applicant concludes that therefore, not only do Taylor et al fail to teach or suggest every element of the methods of the present invention; there are real world disadvantages in performing the methods disclosed by Taylor et al versus the methods claimed in the present invention. Applicant respectfully request that the rejections be withdrawn.

Examiner's Response

6. All of the amendments and arguments filed on October 5, 2004 have been thoroughly reviewed and considered but are not found persuasive for the reasons that follow: In regards to Applicant's arguments that the Taylor et al does not teach the element that "the protein" or "nucleic acid" be in an aqueous solution, the examiner respectfully disagree. Firstly, applicant specification at paragraph 0022, states that "[P]referred methods involve immobilizing the nucleic acid or protein on a substrate which closely simulate solution conditions, such as substrates including a buffer solution, such as a gel. More preferably, the methods utilize a substrate for which there is a direct correlation exists between the thermodynamic parameters of nucleic acids and proteins in the substrate as compared to solution, such as a microchip gel pad".

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In this case, Taylor teaches the use of gel pads arrays. Secondly, Taylor et al teach at column 4, lines 56-57 that "The gel can incorporate reagents, such as polynucleotide probes for capturing fragments of DNA from *a solution*." Applicant appears to only rely on one aspect of the Taylor et al reference and not the reference as a whole. Taylor et al additionally teaches at column 8, beginning at line 28 that "In a preferred embodiment, a biological molecule is attached to the first layer, e.g., a protein or nucleic acid; the biological molecule interacts with a second molecule, e.g., a biological molecule, e.g., a protein that forms a multimeric complex with the immobilized protein, e.g., a protein dimer; or a complex between the immobilized protein and a nucleic acid molecule; e.g., single or double stranded DNA...". Thus, the reference teaches several different forms of interaction between the immobilized molecule and nucleic acid or protein. In response to Applicant's arguments concerning the disadvantages of the Taylor et al method and the advantages of the instant invention, it is noted that the claims comprise "open language" which does not exclude the presence of a two gel layers. While the presence of the two gel layers in Taylor is only one aspect of the reference, arguments concerning the disadvantages of the Taylor reference and the advantages of the instant invention are irrelevant. Specifically such limitations and features Applicant argues are not recited in the rejected or amended claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Applicant's arguments are not sufficient to overcome the prior art rejections. Accordingly, the rejections noted above are maintained.

Claim Rejections - 35 USC § 103

7. One again, claims 1-14, are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al. (US 5,922,617, July 13, 1999) in view of Drobyshev et al (nucleic acids research, Vol. 27, pages 4100-4105, 1999) and further in view of Arenkov et al. (Analytical Biochemistry, Vol. 278, pages 123-131, February 2000). Regarding claims 1-3, 5-6, 8-11, Wang et al. teach a method for characterizing a nucleic acid-protein interaction or a protein-protein interaction, comprising: immobilizing a nucleic acid or a protein on a solid support, (b) contacting the nucleic acid and the protein or the protein and protein under conditions which allow the nucleic acid and the protein to interact; and measuring the strength of the nucleic acid-protein interaction or the protein-protein interaction. (col. 1, lines 66-67 and col. 2, lines 1-14, and col. 7, lines 52-54). The reference further discloses wherein a plurality of different components (nucleic acids or proteins) that are not predetermined sequences are immobilized at different addresses on the solid support and wherein the method steps are repeated to detect interaction between the components (nucleic acid or protein) col. 2, line 60 to col. 3, line 11 and col. 9, lines 24-25; see also col. 17, lines 56-67). Wang et al differ from the instant invention in that the reference does not teach wherein the nucleic acid or protein or immobilized within a gel pad(s).

Drobyshev et al. teach a method of detecting nucleic acid-ligand (dye) interaction comprising the steps of immobilizing a nucleic acid within a gel pad solid support, contacting the nucleic acid and the ligand under conditions which allow the nucleic acid and ligand to interact; and measuring the strength of the nucleic acid-ligand interaction by measuring through T_m or a change in T_m (Abstract and page 4101, Section entitled "Materials and Methods). The reference teaches advantages of using gel pads as an immobilization support in oligonucleotide,

DNA and protein arrays over the use of probes attached to a solid support. Drobyshev et al states that three-dimensional immobilization in gel pads provide higher capacity and a more homogeneous environment than heterophase immobilization on glass or filters (page 4100, col. 2 second full paragraph).

In a similar method to that of Drobyshev et al., Arenkov teaches a method of characterizing protein-protein interaction via the use of a gel pad(s) wherein one of said protein is immobilized within the gel pad microchip (abstract). Arenkov et al provides several advantages of using a microarray of gel-immobilized compounds on a chip such as a gel pad rather than conventional analytical devices, such as that taught by Wang et al. Arenkov et al teach that one advantage of the use of a gel -pad microchip over conventional analytical devices is the possibility of massive parallel analysis. Arenkov et al teach that other advantages of using a gel support for fixation of biological compounds, such as e.g., proteins, is the large capacity for immobilized compounds. Arenkov et al state that the gel pads in an array are separated from each other by a hydrophobic surface, therefore, the gel pads can be used as a large number of individual microtest tubes to carry out specific interactions and chemical and enzymatic procedures (page 123, entire background section). Therefore, in view of the foregoing, one of ordinary skill in the art at the time of the claimed invention would have been motivated to have modified the method of Wang et al to encompass the use of compounds immobilized within a gel pad rather than on a solid surface to characterize nucleic acid or protein interaction. One of ordinary skill in the art at the time of the claimed invention would have been motivated to do so for the advantages taught by Drobyshev et al that gel pads as an immobilization support provides a higher capacity and a more homogeneous environment for analysis. Additionally, one of

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ordinary skill in the art would have been further motivated to have modified the method to encompassed the use of a gel pad as the solid support for the advantages taught by Arenkov that gel pads allow for massive parallel analysis.

Regarding claim 4, Wang et al. teach an embodiment of claim 1, wherein the nucleic acid is ss or ds DNA or RNA (col. 4, lines 10-53).

Regarding claims 12 and 13, Wang et al. teach an embodiment of claim 1, wherein the nucleic acid is a functional nucleic acid sequence, such as a promoter (col. 9, lines 35-40, see also col. 7, lines 41-59).

Regarding claim 14, Wang et al. teach an embodiment of claim 1, wherein the protein (transcription factor) is capable of modulating the activity of a gene or gene product (col. 7, lines 41-59 and col. 9, lines 35-40).

Regarding claims 7, Wang et al. teach an embodiment of claim 1, wherein the strength of the nucleic acid-protein interaction or the protein-protein interaction is measured through fluorescence (col. 7, lines 21-33).

Applicant's Traversal

8. Applicant traverses the rejection on the following grounds: Applicant states that a *prima facie* case of obviousness has not been established. Applicant states that first there is no suggestion of motivation to combine the references cited by the Examiner. Applicant states that the Office Action states that "one of ordinary skill in the art at the time of the claimed invention would have been motivated to have modified the method of Wang et al to encompassed the use of compounds immobilized within a gel pad rather than that on a solid surface to characterized

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nucleic acid or protein interaction. Applicant states that however contrary to the Examiner's assertion, Applicant respectfully submit that because the advantages of the methods found in the Wang et al reference would be lost in combination with the method of Drobyshev et al., the reference in fact teaches away from immobilizing compounds within a gel pad. Applicant states that for example, the methods in Wang et al provide that the immobilized protein or nucleic acid is attached to the solid surface using various specific methods. Applicant asserts that in certain embodiments, these methods provide that "one may use magnetic beads with a magnetic or magnetizable solid support. Applicant states that Wang et al go on further to state that "using the various techniques of this invention, particularly the magnetic beads, provides great flexibility, where the bound components can be arrayed in any number of sizes and with the bead, the arrays are reversible and can be retrieved for further processing. Applicant states that the skilled artisan can immediately see the advantages to arrays that are reversible, such as being useful in releasing particular molecules from the surface during the assay, or using the same assay more than once while limiting the bound areas of the assay during the subsequent use. Applicant states that furthermore, there are other advantages known in the art to using an impermeable, rigid support instead of a gel pad. Applicant states that for example, because liquid cannot penetrate the surface of the solid support, target nucleic acids can find immediate access to the probes without diffusing into pores. Applicant states that this enhances the rate of hybridization...[t]he washing step which follows hybridization is also unimpeded by diffusion, speeding up the procedure and improving reproducibility". Applicant states that as the skilled artisan would understand that the would be giving up as many (or more) advantages by using the gel pads with the methods of Wang et al., it is highly unlikely that one would take the teachings

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of Wang et al and combine them with the teachings of Drobyshev et al and Arenkov et al to use gel pads. Applicant states that the methods in Wang et al and the methods of the present invention simply provide advantages that are opposed to each other. Applicant states that one seeking the advantages of Wang et al would not use the present invention and vice-versa. Applicant concludes that there is no motivation to combine and in fact there are many motivations not to combine the references cited by the Examiner. Applicant states that because there is no motivation to combine the teachings, a *prima facie* case of anticipation has not been established. Applicant request the rejection be withdrawn.

Examiner's Response

9. Applicants arguments filed on October 5, 2004 have been thoroughly reviewed and considered but are not found persuasive for the reasons that follows: In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the primary reference of Wang et al teaches the limitations of the reference as noted above. Wang differs from the instant invention in that the reference does not teach wherein the nucleic acid or protein immobilized on the solid support is immobilized within a gel pad(s). However the reference teaches that the solid support may take many forms, limited to the ability to segregate components, address sites of the solid substrates to determine the occurrence of events, provide

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for stability of the distribution of the bound components and the interaction with the mobile components, ease of production and the like (col. 11-16). The secondary reference of Drobyshev et al teach a method of detecting nucleic acid-ligand interaction using a gel pad solid support having nucleic acid immobilized therein. Drobyshev et al further teach that gel pads provides essential advantages as an immobilization support in oligonucleotide, DNA and protein array over the use of probes attached to a glass solid support. The reference teaches that three-dimensional immobilization in gel pads provide higher capacity and a more homogeneous environment than heterophase immobilization on glass or filters and allows for massive screening of the sequence specificity of DNA-binding compounds. The tertiary reference of Arenkov provides a similar teaching to that of Drobyshev and provides further motivation for using a gel pad solid support instead of a rigid solid support. Arenkov et al teach that gel pads proves a much higher capacity for immobilization over a tow dimensional glass or plastic surface, homogeneous water environment for immobilized proteins and some other essential advantages. The reference teaches that immobilized proteins are well spaced and do not interact with each other or with the glass surface. Arenkov et al teach that this prevents the aggregation of immobilized proteins or their interphase-induce denaturation on a solid surface (page 130, last paragraph of col. 1 bridging first paragraph of col. 2). Additionally, Arenkov et al teach that gel pads are also advantageous for the capability of massive parallel analysis of proteins in specific interactions or in chemical and/or enzymatic procedures. Thus based on the advantages noted above in the teaching of Drobyshev et al and Arenkov et al, one of ordinary skill in the art at the time of the claimed invention would have been motivated to have perform the method of detecting protein-nucleic acid interaction as taught by Wang et al using other forms of solid

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support besides a glass or beads, such as a gel pads. One of ordinary skill in the art would have been motivated to so for the advantages taught by both Drobyshev et al and Arenkov et al that gel pads as an immobilization support provides a higher capacity and more homogeneous environment for analysis of specific interactions and additionally allows for massive parallel analysis and based on the teaching of Wang that any form of solid support can be used in the method of detecting nucleic acid-protein interactions.

In regards to Applicant's arguments concerning the advantages of using a rigid support instead of a gel pad, the Examiner acknowledges Applicant's arguments and citation of the Southern et al non-patented literature. However, while there are noted advantages for using a rigid support instead of a gel pad, there are also noted advantages for using a gel pad instead of a rigid support. These advantages have been noted in the prior Office action and noted above. Thus contrary to Applicant's arguments the secondary and tertiary references provides valid motivation for wanting to utilize a gel pad instead of a rigid solid support. Likewise, the reference of Wang is not limited to only a rigid solid support because the reference states that the solid support can take any form as long as it allows for the ability to segregate components, address sites of the solid substrates to determine the occurrence of events, provide for stability of the distribution of the bound components and the interaction with the mobile components, ease of production and the like (col. 11-16). In this case the secondary and tertiary reference teaches wherein that the gel pads are capable of such functions. Therefore, Applicant's arguments are not sufficient to overcome the prior art rejection. Accordingly, the rejections under 35 USC 103(a) are maintained.

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10. Once again, claims 15, 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guschin et al as previously discussed above in view of Ahern et al. Regarding claims 15, 16, Guschin et al. teach a method for characterizing a nucleic acid-protein interaction or a protein-protein interaction, comprising: immobilizing a nucleic acid or a protein on a solid support, (b) contacting the nucleic acid and/or the protein under conditions which allow the nucleic acid and the protein to interact; and measuring the strength of the nucleic acid-protein interaction or the protein-protein interaction. Guschin et al. differ from the instant invention in that the reference does not teach the method is in the form of a kit. However, Guschin et al. teach reagents that would be necessary in the kit such as solid support, buffers and dyes. In a scientific article, Ahern teaches the advantages of using a kit. Ahern teaches that a kit provides convenience, time management and ease of practicing to the investigator (page 4, second-fourth paragraphs). Therefore, in view of the teachings of Ahern, one of ordinary skill in the art would have been motivated at the time of the claimed invention to have modified the nucleic acid and/or protein interaction as taught by Guschin et al to encompass a kit. One of ordinary skill in the art would have been motivated to do so for the advantages taught by Ahern that a kit provides convenience, time management and ease of practicing to the investigator.

Applicant's Traversal

11. Applicant traverses the rejections on the following grounds: Applicant states that Guschin et al simply do not teach every element of the claimed invention as discussed previously above. Applicant states that a review of the reference of Guschin et al fails to reveal or disclose an interaction between a nucleic acid and a protein, such as required by (b) of amended claim 1, the independent claim from which both claim 15 and 16 depends. Applicant states that the Ahern

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reference, a description of a kit containing simple pre-made reagents fails to cure the deficiency of Guschin et al. Applicant states that moreover, the examiner has pointed to no suggestion or motivation to modify either reference to supply the missing elements. Applicant concludes that the a prima facie case of obviousness regarding claim 15 and 16 has not been met and respectfully request the rejection be withdrawn and allow the claims to issue.

Examiner's Response

12. The examiner acknowledges Applicant's arguments, however it is noted that the claims are drawn to a product comprising instructions, one or more solid support, buffer, dyes or disposable lab equipment. The "for characterizing nucleic acid-protein interactions" and "for carry out the method of claim 1" is an intended use limitation. MPEP states that recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). In this case, the reference of Guschin teaches reagents for the product of claims 15 and 16 that are capable of functioning in the same manner as that claimed in the instant invention. Guschin et al does not teach wherein the products are in the form of a kit. The secondary reference of Ahern is submitted to provide motivation for wanting the reagents of Guschin et al in the form of a kit. As noted in the prior Office action, Ahern teaches that a kit provides ease and convenience of practicing to the practitioner. Therefore, one of ordinary skill in the art would have been motivated to provide the reagents as taught by

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Guschin et al in the form of a kit for the advantages taught by Ahern as noted above and previous Office Action.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, motivation to combine the references is provided in the secondary reference of Ahern as discussed earlier. Applicant's arguments are not sufficient to overcome the prior art rejection. Accordingly, the rejections under 35 USC 103(a) are maintained.

Conclusion

13. No claims are allowed. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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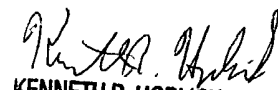
14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be emailed to cynthia.wilder@uspto.gov. Since email communications may not be secure, it is suggested that information in such request be limited to name, phone number, and the best time to return the call.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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KENNETH R. HORLICK, PH.D.
PRIMARY EXAMINER

12/22/04